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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/831,307	01/07/2002	Stephen Kent	229752001400	2826
25227	7590	03/13/2006	EXAMINER	
MORRISON & FOERSTER LLP 1650 TYSONS BOULEVARD SUITE 300 MCLEAN, VA 22102			PARKIN, JEFFREY S	
		ART UNIT	PAPER NUMBER	
		1648		

DATE MAILED: 03/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/831,307	KENT ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Jeffrey S. Parkin, Ph.D.	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### **Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

1)  Responsive to communication(s) filed on 19 December 2005.

2a)  This action is **FINAL**.                            2b)  This action is non-final.

3)  Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

4)  Claim(s) 1,17-19,24,25,30,31 and 38 is/are pending in the application.  
4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5)  Claim(s) \_\_\_\_\_ is/are allowed.

6)  Claim(s) 1, 17-19, 24, 25, 30, 31, and 38 is/are rejected.

7)  Claim(s) \_\_\_\_\_ is/are objected to.

8)  Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

9)  The specification is objected to by the Examiner.

10)  The drawing(s) filed on \_\_\_\_\_ is/are: a)  accepted or b)  objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)  The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)  Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a)  All b)  Some \* c)  None of:  
1.  Certified copies of the priority documents have been received.  
2.  Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3.  Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1)  Notice of References Cited (PTO-892)  
2)  Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3)  Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date

4)  Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_ .

5)  Notice of Informal Patent Application (PTO-152)

6)  Other: \_\_\_\_\_

Serial No.: 09/831,307  
Applicants: Kent, S., et al.

Docket No.: 229752001400  
Filing Date: 01/07/02

#### **Detailed Office Action**

##### **37 C.F.R. § 1.114**

A request for continued examination under 37 C.F.R. § 1.114, including the fee set forth in 37 C.F.R. § 1.17(e), was filed in this application after final rejection on 19 December, 2005. Since this application is eligible for continued examination under 37 C.F.R. § 1.114, and the fee set forth in 37 C.F.R. § 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 C.F.R. § 1.114.

##### ***Status of the Claims***

Claims 1, 17-19, 24, 25, 30, 31, and 38 are pending in the instant application.

##### **37 C.F.R. § 1.75(c)**

Claim 38 is objected to under 37 C.F.R. § 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claims in proper dependent form, or rewrite the claim(s) in independent form. The claim fails to distinguish over claim 1. Both claims comprise a recombinant fowlpox vector encoding a heterologous antigen and cytokine. Although claim 38 is directed toward an agent, the claim fails to set forth any distinguishing characteristics that make it patentably distinct from claim 1. Refer to M.P.E.P. § 608.01(n).

##### **35 U.S.C. § 103(a)**

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not

identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1, 17-19, and 38 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Paoletti et al. (1998) in view of Ramshaw et al. (1999). The claims are directed toward a fowlpox virus vector encoding a heterologous antigen (e.g., HIV Gag and/or Pol) and cytokine (e.g.,  $\gamma$ -IFN) and methods of using said vector to induce a viral-specific immune response. Paoletti and colleagues provide **fowlpox** viral vectors (e.g., **TROVAC**) encoding lentiviral (e.g., **HIV**, SIV) gene products (e.g., Gag, Pol, Env) that are suitable for inducing viral-specific immune responses (see col. 5, lines 19-36; col. 7, lines 1-20; cols. 153-154). This teaching does not disclose the utilization a second nucleic acid encoding a cytokine that functions as an adjuvant. However, the claims do

specify that attenuated pox viruses may be administered with both the heterologous antigen and an adjuvant.

Ramshaw and colleagues provide recombinant viral vectors (e.g., **poxviruses**) carrying a first nucleic acid encoding a viral immunogen (e.g., **HIV-1**) and a second nucleic acid encoding a cytokine adjuvant (e.g., IL-2,  $\gamma$ -IFN) that facilitates the immune response to the immunogen (see abstract; col. 2, lines 6-41; col. 3, lines 34-55; col. 4, lines 27-34 and 44-58; col. 5, lines 5-33 and 60-65). Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to modify the fowlpox expression vector of Paoletti et al. (1998), to include a second nucleic acid encoding a cytokine adjuvant as taught by Ramshaw et al. (1999), since this would reasonably be expected to enhance the immune response to the HIV-1 antigen of interest. Both the motivation and a reasonable expectation of success were clearly present in the prior art.

Applicants traverse and submit that there is no motivation to arrive at the claimed invention. This position is clearly untenable in view of the prior art. As previously set forth, there is no question that Ramshaw et al. (1999) teach that the inclusion of a nucleotide sequence encoding a **cytokine** (e.g., IL-2,  $\gamma$ -IFN), as well as, a nucleotide sequence encoding a **heterologous antigen** (e.g., HA), in the genetic background of a poxvirus (e.g., vaccinia virus) results in strong immune response against the heterologous antigen. The authors unambiguously state (see col. 2, lines 22-36) that "the co-expression of the lymphokine with the antigenic polypeptide(s) ensures that on administration of the vaccine the lymphokine and antigenic polypeptide(s) are delivered together at the same time and at the same site, giving an improved immune response to the antigenic polypeptide(s)." The only limitations of this teaching is that it does not disclose a fowlpox virus construct or a heterologous HIV antigen. However, the inventors

state that the antigenic polypeptide may be "derived from the human immunodeficiency virus (HIV), together with a second nucleotide sequence capable of being expressed as all or an active part a lymphokine effective at enhancing or modifying the immune response of the individual to the HIV antigenic polypeptide" (col. 3, lines 43-50) and that other poxvirus vaccine vectors may be employed (col. 5, lines 60-65). Paoletti and colleagues provide fowlpox viral vectors (e.g., **TROVAC**) encoding lentiviral (e.g., **HIV**, SIV) gene products (e.g., Gag, Pol, Env) that are suitable for inducing viral-specific immune responses (e.g., see Example 3). Thus, contrary to applicants' assertions, there would have been more than sufficient motivation to modify the compositions of Paoletti et al. (1998), to include a second nucleic acid encoding a cytokine adjuvant as taught by Ramshaw et al. (1999), since this would reasonably be expected to enhance the immune response to the HIV-1 antigen of interest. Contrary to applicants' assertion, both the motivation and a reasonable expectation of success were clearly present in the prior art. Moreover, applicants have failed to proffer any evidence that would teach away from the claimed invention.

Applicants further suggest that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning. Applicants are reminded that it must be recognized that any judgement on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. *In re McLaughlin*, 443 F.2d 1392; 170 U.S.P.Q. 209 (C.C.P.A. 1971). As set forth *supra*, there was clearly sufficient motivation to include a second gene encoding a cytokine, such as  $\gamma$ -IFN, in a fowlpox recombinant vaccine vector since it was clearly

emphasized that this would lead to the development of strong immune response against the immunogen of interest.

***35 U.S.C. § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24, 25, 30, and 31 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are all directed toward HIV vaccine compositions, methods of making said compositions, and attendant methods of use to prevent HIV transmission or provide a therapeutic response in HIV-infected individuals. The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. *Enzo Biochem, Inc.*, 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). *In re Wands*, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). *Ex parte Forman* 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). As previously set forth, the courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965).

The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

- 1) The state-of-the-art relative to HIV vaccine development is replete with failure.** The development of an efficacious HIV vaccine has proven to be arduous. There are a number of factors that have precluded the successful development of an HIV vaccine including some of the following: (i) a lack of understanding of the correlates of protective immunity; (ii) a lack of understanding of protective immunogens, suitable adjuvants, routes of administration, and immunization regimens; (iii) the quasispecies nature of HIV replication leads to immune escape and effete immune responses; and (iv) the lack of an adequate animal model in which to assess vaccine efficacy (Haynes et al., 1996; Lee, 1997; Letvin, 1998; Burton and Moore, 1998; Johnston, 2000; Feinberg and Moore, 2002).
- 2) The disclosure fails to provide adequate guidance pertaining to the correlates of protective immunity.** In order to assess the effectiveness of any given putative vaccine, the skilled artisan needs to know the specificity and titer of those immune responses that induce protection or provide some sort of therapeutic effect. However, to date these correlates are not known and the disclosure fails to provide any further illumination on the subject. Thus, the skilled artisan cannot reasonably ascertain if any given putative vaccine composition will be protective.
- 3) The disclosure fails to provide adequate guidance pertaining to suitable immunogens, adjuvants, routes of administration, and immunization regiments.** Since the correlates of protective immunity remain to be elucidated, the skilled artisan cannot begin to predict which form the immunogen of interest should take (i.e., whole inactivated virus; live attenuated virus; subunit immunogen; combination of multiple immunogens in various forms), the appropriate adjuvants to be included, suitable routes of

administration, or suitable immunization regimens. The disclosure fails to provide any further illumination on the subject.

**4) The disclosure fails to provide any working embodiments.** While it was noted that the specification described challenge studies involving one of the claimed compositions and a macaque model, many of the parameters of this study were not clearly disclosed (i.e., challenge virus, inoculating dose, etc.). In any event, the macaque model is clearly not predictive of clinical efficacy due to the various genotypic and phenotypic differences between macaques, humans, and the lentiviruses that infect them. Accordingly, when all the aforementioned factors are considered *in toto*, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

Applicants again traverse and submit that the disclosure fully supports the breadth of the claimed invention. This position is clearly untenable in view of the state-of-the-art vis-à-vis HIV vaccine development. The crux of the rejection is not whether or not the claimed compositions could be prepared, but whether they would provide an immune response capable of preventing or treating HIV infection. As set forth *supra*, HIV vaccine development is characterized by unpredictability. The correlates of protection remain to be elucidated. Adequate animal models that can be used to assess vaccine efficacy do not exist. Moreover, numerous clinical trials have resulted in failure. Applicants' response again fails to proffer any data that addresses the aforementioned concerns. Accordingly the rejection is proper and hereby maintained.

#### **Correspondence**

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571)

272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D.  
Primary Examiner  
Art Unit 1648

06 March, 2006